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isotope a prime candidate for several personalized nuclear medicine applications.
This isotope can be produced in large quantities as a low specific activity (up to 800 GBq/g) product in reactors via the Sn-116(n,γ) or Sn-117(n,n'γ) reactions. A carrier-free, high specific activity (up to 800 TBq/g) isotope can be manufactured with ~50 MeV cyclotrons employing either Sb(p,x) or Cd-116(α,3n). Methods for extracting and purifying the Sn-117m from Sb or Cd have been developed.
Sn-117m has been used to label a wide variety of targets including proteins, anti-bodies and small molecules. In recent animal and human Phase I/II cardiovascular trials to detect and treat vulnerable plaque, the Sn-117m was chelated to aminobenzyl DOTA before being conjugated to annexin V. Results demonstrated the ability of this molecule to both target and image the plaques. Additionally, a remarkable therapeutic effect was observed at very low doses (~10 cGy).
In oncology, Sn-117m (chelated to DTPA) has been successfully used in over 120 humans for bone pain palliation in a Phase I/II trial. Labeling of neuroendocrine cancer targeting molecules has also been demonstrated. The isotope, in low specific activity form, has been electroplated onto stents and implanted into several animal models to demonstrate the efficacy and finite range of the conversion electrons. Human and veterinary applications are under development.
Rheumatological applications include a homogeneous Sn-117m colloid that is being used to treat (radiosynoviorthesis) canine osteoarthritis (OA). Future veterinary applications include treating equine OA and human rheumatoid arthritis (RA). Labeled compounds are also being developed to image and treat RA systemically.
Additional future applications being explored take advantage of the limited irradiation of normal tissue in immune and inflammatory CNS conditions that could provide new therapeutic advantages to this immunologically privileged system. In conclusion, the novel isotope Sn-117m is successfully finding application in several aspects of human nuclear medicine and is now also creating new opportunities in the emerging field of veterinary nuclear medicine.

Keywords: Sn-117m, manufacturing, nuclear medicine applications

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A comprehensive omics approach for development of prognostic or predictive biomarkers in squamous cell carcinoma of the head and neck treated with radiation
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Purpose: We have taken a comprehensive approach to develop biomarkers of potential therapeutic radioresponse. This approach includes gene, miRNA, and protein expression, as well as methylation and mutation analysis. Methods: Specimens from 102 HNSCC patients identified by surgical and pathologic criteria considered high risk for local recurrence (LR) or distant metastasis (DM) after post-operative radiotherapy as well as 22 specimens from adjacent normal tissue were used. We have strived to avoid the pitfalls of biomarker discovery such as inadequate clinical phenotyping, the use of specimens of convenience, poorly annotated specimens, heterogeneous specimens and underpowered sample sets amongst others.
Results: While a 46 gene signature was able to stratify patients based upon risk for overall survival, no gene signature was able to segregate specimens specific to LR or DM. This 46 gene signature, however, was able to stratify patients by overall survival in this data set, 5 independent HNSCC data sets as well as the TCGA data set. However, using a 36 miRNA signature PORT outcomes (LR or DM could be predicted. Unfortunately, when applied to the TCGA data set 13 miRNA were unavailable limiting the external validation to survival only. DNA methylation analysis, which is still ongoing, has identified DM and LR and includes genes in pathways associated with EMT and DNA repair, respectively. We have also taken the approach that biomarkers should have a biological basis and we have examined a set of 49 HNSCC cells lines for gene and miRNA expression, and methylation. Furthermore, full radiation survival curves were generated. Filtering through miRNA target databases and examining negative correlations of miRNA and gene expression led to the isolation of several miRNA for further analysis. For example, miR-125a was under-represented in the LR cohort. miR-125a is a negative prognostic indicator in gastric cancer, targeting ERBB2. ERBB2 gene expression is anti-correlated with miR-125a expression in tumor specimens and in our 49 HNSCC cell lines. Furthermore, up-regulation of miR-125a in HN5 cells led to radiosensitization while down-regulation of miR-125a led to radioresistance. Within the DM group, miR-551a and 551b-3p are over-represented. These miRNA drive cell proliferation, migration and invasion. A target of these miRNA is GLIPR2. The GLIPR2 protein binds BCLN1 and sequesters it within the golgi. Release of BCLN1 allows cells to enter into autophagy and by modulating miRs 551a and 551b-3p, we can drive cells into autophagy, enhance invasiveness and increase radioresistance.
Conclusions: The expression of miRs 551a and 551b-3p as well as GLIPR2 gene expression can stratify patient outcome in our patient cohort, other HNSCC cohorts as well as other invasive cancers. Their expression is also highly associated with late stage HNSCC. Lastly, we are now integrating data sets to take a panomics approach to biomarker development.

Keywords: head and neck cancer, omics, radiation therapy, biomarkers

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Development of a High Resolution Module for PET scanners
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Purpose: PET ("Positron Emission Tomography") scanners have to guarantee high performances in term of spatial resolution and sensitivity allowing to detect cancer mass while it is still sufficiently small and has not had time to spread to other parts of the body. in this frame we focused on the development of the scintillator module that can reach high performance as compared to the current scanners and at the same time that keeps low costs and not complex design. To guarantee high performance in term of spatial resolution, the Depth of Interaction (DOI) information has to be reached. Instead of using the usual approach, with a double side readout, to have DOI capability we have developed a new PET module that can provide the DOI information using just a single side readout.
Materials and Method: The module presented is based on a 64 LYSO ("Lutetium-yttrium oxyorthosilicate") crystals matrix and on an MPPC ("Multi Pixels Photon Counter") as detector that guarantee a 4 to 1 coupling between the crystals and the detector and a single side readout. The lateral surfaces of the crystals are optically processed. Different configuration with light guide between the MPPC and the crystals matrix The readout of the signal is performed by a digitizer that record for each trigger event the charge collected by each MPPC after the integration of the signal. The digitizer is connected to a custom designed acquisition card that provides at the same time bias voltage to all the MPPC channels. The matrix is fixed to the board using a PVC custom made holder that also keep all the parts of the module in place. To characterize the module a ^{22}Na radioactive source is placed 2 cm above the matrix exciting the scintillators. To test the DOI capability of the module a LYSO crystal is placed on the opposite side of the source allowing to illuminate a given vertical portion of the crystals and to permit to scan the vertical length of the module.
Results: Combinations of the collected charge can be used to